

Supplementary Online Content

Horton DB, Scott FI, Haynes K, et al. Antibiotic exposure, infection, and the development of pediatric psoriasis: a nested case-control study. *JAMA Dermatol*. Published online November 11, 2015. doi:10.1001/jamadermatol.2015.3650.

eFigure 1. Timing of Rashes Noted by General Practitioners Relative to Psoriasis Diagnosis

eFigure 2. Sensitivity Analysis: Association of Antibiotics, Infections, and Psoriasis With Varying Index Dates

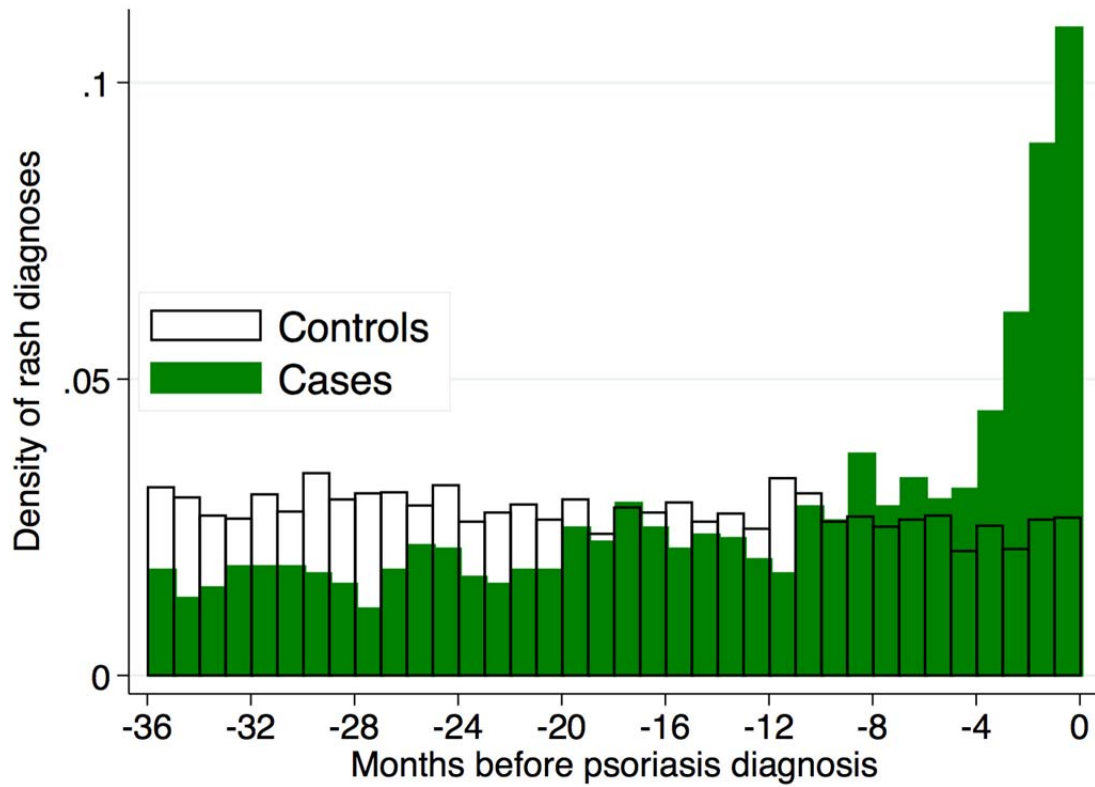
eTable 1. Characteristics of Participants With Psoriasis

eTable 2. Secondary Analysis of the Association of Antibiotics, Infections, and Psoriasis

eTable 3. Sensitivity Analysis of the Association of Antibiotics, Infections, and Psoriasis

This supplementary material has been provided by the authors to give readers additional information about their work.

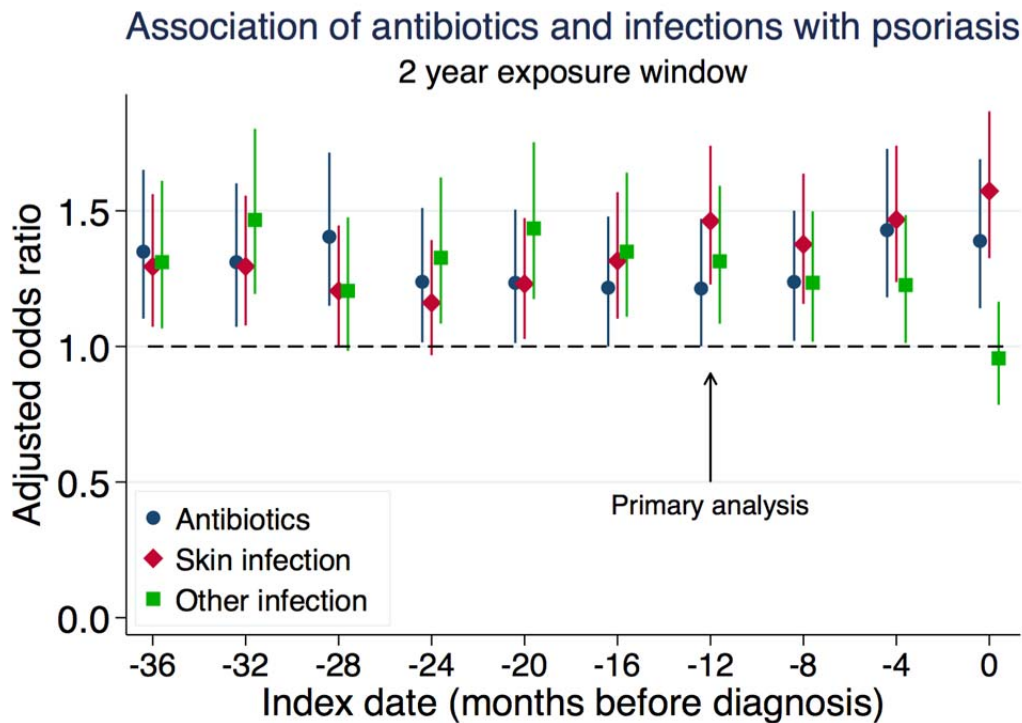
eFigure 1. Timing of Rashes Noted by General Practitioners Relative to Psoriasis Diagnosis



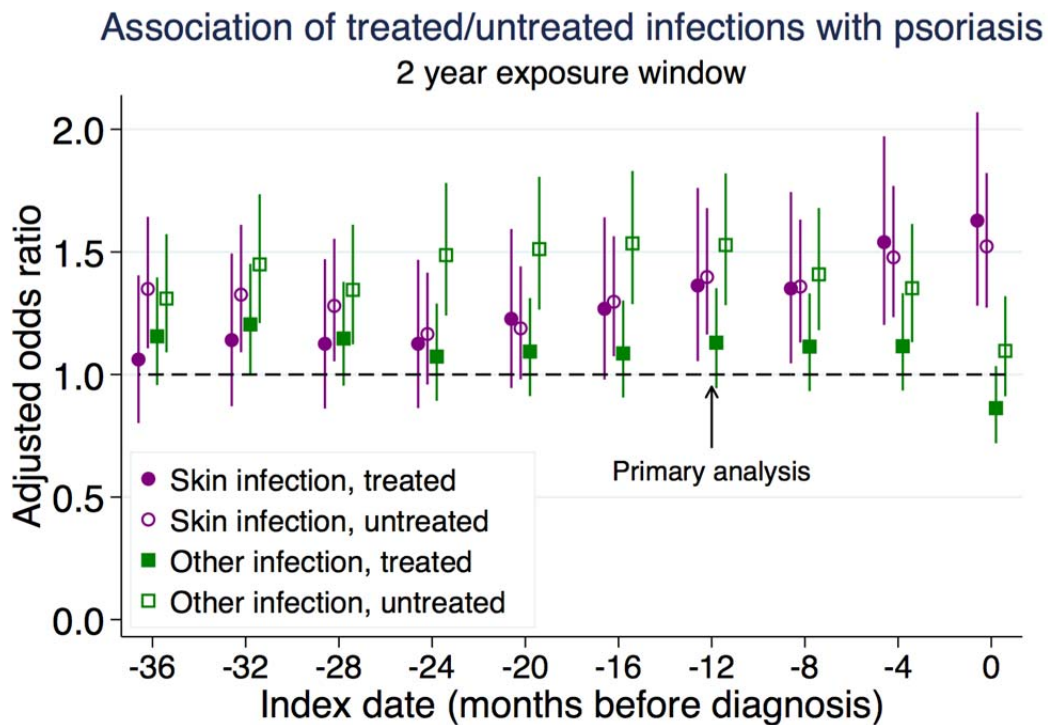
All columns total density=1 for each group, cases and controls. The lower density of rashes among cases 12-36 months before diagnosis reflects the higher density of rashes closer to diagnosis, not lower absolute rates of rash compared with controls.

eFigure 2. Sensitivity Analysis: Association of Antibiotics, Infections, and Psoriasis With Varying Index Dates

A



B



eTable 1. Characteristics of Participants With Psoriasis

Psoriasis characteristics	N (%)
Clinical variant	
Guttate psoriasis	160 (18.9)
Pustular	4 (0.5)
Other	3 (0.4)
Not otherwise specified	678 (80.2)
Psoriasis drug use, any ^a	
Topical, any	746 (88.3)
Calcineurin inhibitor	27 (3.2)
Coal tar	221 (26.2)
Dithranol	12 (1.4)
Glucocorticoid	644 (76.2)
Vitamin D analog	206 (24.4)
Immunosuppressant	6 (0.7)
Phototherapy	3 (0.4)
Secondary outcome definitions ^a	
Any psoriasis + psoriasis drug	747 (88.4)
Any psoriasis + dermatology referral	213 (25.2)

^a Some subjects had more than one type.

eTable 2. Secondary Analysis of the Association of Antibiotics, Infections, and Psoriasis

	Exposed cases	Exposed controls	Unadj. odds ratio	Adjusted odds ratio, 95% CI	P value	Exposed cases	Exposed controls	Unadj. odds ratio	Adjusted odds ratio, 95% CI	P value
Model, exposure variables	2 year exposure window					Lifetime exposure window				
Stratification by infection history^a										
Any antibiotic, among those without prior documented infection	N=262	N=1483	2.0	1.2	0.34	N=88	N=533	1.5	1.3	0.58
	46	126		(0.8, 1.9)		21	74		(0.6, 2.9)	
Any antibiotic, among those with prior documented infection	N=556	N=2966	1.2	1.1	0.60	N=556	N=2966	1.9	1.5	0.003
	407	2121		(0.8, 1.3)		508	2587		(1.2, 2.0)	
Adjustment for additional covariates^b	N=741	N=6510				N=741	N=6510			
Any antibiotic, adjusted for maternal history of autoimmune disease	408	2659	1.9	1.2	0.09	623	4893	2.1	1.5	0.003
				(0.97, 1.5)					(1.1, 2.0)	
Any antibiotic, adjusted for maternal history of psoriasis	408	2659	1.9	1.2	0.10	623	4893	2.1	1.5	0.004
				(0.97, 1.5)					(1.1, 1.9)	
Coverage of antimicrobial^{c, d}	N=818	N=7913				N=818	N=7913			
Any antianaerobic antibiotic prescription	399	2929	1.7	1.1	0.35	660	5725	1.9	1.3	0.01
				(0.9, 1.3)					(1.1, 1.7)	
Any non-antianaerobic antibiotic prescription	149	1018	1.5	1.0	0.83	346	2650	1.5	1.2	0.07
				(0.8, 1.3)					(0.99, 1.4)	
Any non-bacterial antimicrobial prescription	31	266	1.2	0.8	0.27	80	638	1.2	1.0	0.96
				(0.5, 1.2)					(0.8, 1.3)	
Secondary case definitions^c										
Psoriasis + drug for	N=723	N=6987				N=723	N=6987			

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<u>psoriasis</u>										
Any antibiotic prescription	413	2913	2	1.2	0.03	611	5267	2.1	1.5	0.006
				(1.02, 1.5)					(1.1, 1.9)	
Any skin infection ^e	231	1368	2	1.5	<0.001	416	3179	1.8	1.4	<0.001
				(1.3, 1.8)					(1.2, 1.7)	
Any other infection ^f	420	3023	2	1.3	0.005	637	5741	1.8	1.1	0.36
				(1.1, 1.6)					(0.9, 1.5)	
<u>Psoriasis + dermatology referral</u>	N=201	N=1944				N=201	N=1944			
Any antibiotic prescription	119	813	2.2	1.6	0.02	168	1450	2	1.7	0.05
				(1.1, 2.4)					(1.00, 2.8)	
Any skin infection ^e	56	356	1.8	1.4	0.05	114	839	2	1.7	0.002
				(1.00, 2.0)					(1.2, 2.2)	
Any other infection ^f	116	865	1.8	1.1	0.75	169	1591	1.2	0.7	0.12
				(0.7, 1.6)					(0.4, 1.1)	

^a Models adjusted for matching, country, deprivation score, and number of outpatient visits.

^b Models also adjusted for matching, skin and non-skin infections, country, deprivation score, number of outpatient visits, and additional covariates (family history) as noted.

^c Models adjusted for antibiotic exposure, skin infections and non-skin infections, along with matching, country, deprivation score, and number of outpatient visits.

^d Antianaerobic antibiotics: penicillins, broad-spectrum penicillins, metronidazole, clindamycin tetracyclines, glycopeptides (oral vancomycin), carbapenems, cefoxitin (all other cephalosporins categorized as non-antianaerobic). Non-antianaerobic antibiotics: cephalosporins, macrolides, sulfonamides, fluoroquinolones, and all other antibiotic classes. Non-bacterial antimicrobials: systemic antifungal, antimalarial, antimycobacterial, and antiviral drugs.

^e Includes external genitourinary, herpes simplex, molluscum, tinea, varicella, other acute viral exanthems, warts, and other skin or soft tissue infections.

^f Includes upper and lower respiratory, gastrointestinal, urinary tract, and all other infections.

eTable 3. Sensitivity Analysis of the Association of Antibiotics, Infections, and Psoriasis

	Exposed cases	Exposed controls	Unadj. odds ratio	Adjusted odds ratio, 95% CI	P value	Exposed cases	Exposed controls	Unadj. odds ratio	Adjusted odds ratio, 95% CI	P value
Model, exposure variables	2 year exposure window					Lifetime exposure window				
Assume antibiotics received with hospitalization for infection ^a	N=818	N=7913				N=818	N=7913			
Any antibiotic prescription	457	3284	1.9	1.2	0.03	691	5967	2.2	1.7	0.001
				(1.02, 1.5)					(1.2, 2.0)	
Any skin infection ^b	248	1531	1.9	1.5	<0.001	465	3616	1.7	1.4	<0.001
				(1.2, 1.7)					(1.2, 1.7)	
Any other infection ^c	466	3438	1.9	1.3	0.007	712	6515	1.6	1	0.97
				(1.1, 1.6)					(0.8, 1.3)	
Skin infection ^b , treated	86	502	1.7	1.4	0.02	219	1551	1.6	1.3	0.009
				(1.1, 1.8)					(1.1, 1.5)	
Skin infection ^b , untreated	188	1178	1.7	1.4	<0.001	391	3003	1.6	1.3	0.001
				(1.2, 1.7)					(1.1, 1.6)	
Other infection ^c , treated	298	2122	1.6	1.1	0.13	582	4823	1.7	1.3	0.006
				(0.96, 1.4)					(1.1, 1.6)	

Other infection ^c , untreated	362	2452	1.9	1.5	<0.001	658	5871	1.5	1.1	0.28
				(1.3, 1.8)					(0.9, 1.4)	
Cases defined by having two or more psoriasis codes^a	N=239	N=2308				N=239	N=2308			
Any antibiotic prescription	149	997	2.3	1.2	0.35	216	1815	3.1	1.8	0.03
				(0.8, 1.7)					(1.1, 3.2)	
Any skin infection ^b	91	463	2.5	1.9	<0.001	156	1098	2.3	1.8	<0.001
				(1.4, 2.6)					(1.3, 2.5)	
Any other infection ^c	155	1008	2.6	1.8	0.002	220	1938	2.5	1.4	0.31
				(1.2, 2.5)					(0.8, 2.4)	
Skin infection ^b , treated	31	156	2.1	1.4	0.13	71	469	1.7	1.3	0.1
				(1.3, 2.5)					(0.95, 1.8)	
Skin infection ^b , untreated	73	358	2.4	1.8	<0.001	133	898	2.1	1.7	0.001
				(1.3, 2.5)					(1.2, 2.3)	
Other infection ^c , treated	103	645	2	1.4	0.04	189	1455	2.4	1.7	0.007
				(1.02, 1.9)					(1.2, 2.4)	
Other infection ^c , untreated	121	706	2.5	1.8	<0.001	207	1742	2.3	1.3	0.24
				(1.3, 2.5)					(0.8, 2.0)	
Controls	N=845	N=8379				N=845	N=8379			

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matched on age, sex, and practice^d										
Any antibiotic prescription	453	3433	1.8	1.2	0.07	686	6143	1.9	1.3	0.02
				(0.98, 1.4)					(1.04, 1.7)	
Any skin infection ^b	248	1652	1.7	1.3	0.002	465	3705	1.7	1.4	<0.001
				(1.1, 1.6)					(1.2, 1.6)	
Any other infection ^c	466	3623	1.7	1.2	0.07	712	6583	1.6	1.1	0.51
				(0.98, 1.4)					(0.8, 1.4)	
Skin infection ^b , treated	84	557	1.6	1.2	0.22	216	1592	1.5	1.2	0.03
				(0.9, 1.5)					(1.02, 1.5)	
Skin infection ^b , untreated	190	1283	1.6	1.3	0.008	392	3083	1.5	1.3	0.004
				(1.1, 1.5)					(1.1, 1.5)	
Other infection ^c , treated	293	2208	1.6	1.1	0.2	573	4896	1.7	1.3	0.02
				(0.9, 1.3)					(1.04, 1.5)	
Other infection ^c , untreated	366	2581	1.9	1.4	<0.001	664	5901	1.7	1.3	0.02
				(1.2, 1.7)					(1.04, 1.6)	

^a Models adjusted for exposure variables shown as well as matching, country, deprivation score, and number of outpatient visits.

^b Includes external genitourinary, herpes simplex, molluscum, tinea, varicella, other acute viral exanthems, warts, and other skin or soft tissue infections.

^c Includes upper and lower respiratory, gastrointestinal, urinary tract, and all other infections.

^d Models adjusted for exposure variables shown as well as matching and number of outpatient visits.